PROSTATE BRACHYTHERAPY

UK & Ireland Conference 2018

The Spa Hotel, Tunbridge Wells
Friday 23rd March 2018

Platinum sponsor

BXTAccelyon®

ADT in brachytherapy

Adding efficacy or just toxicity

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Europe Hospitals Brussels - Belgium

Localized prostate cancer: heterogeneous group of tumours

Prognostic 'risk' groups: Low – Intermediate - High

Depending on:

- Extension of the tumour
- Initial PSA
- Gleason Score

Low Risk

Stage: T1 or T2a,b
Gleason Sum ≤ 6
PSA ≤ 10 ng/ml

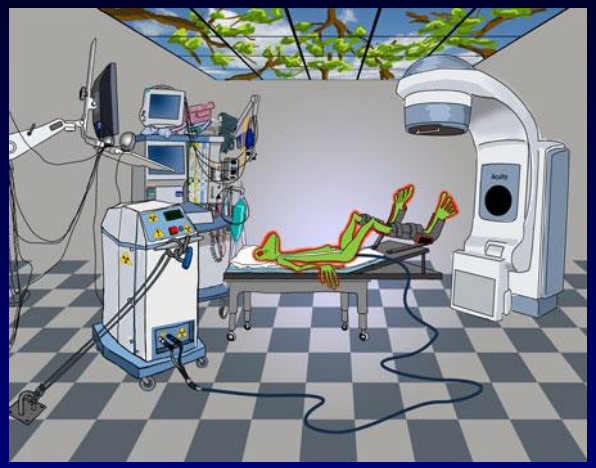
Intermediate Risk

Stage T1 or T1-2 — Gleason Score 7 — PSA < 10
or
Stage T1-2 — Gleason 6 — PSA 10-20

High Risk

Stage T2c or T3
Gleason score ≥ 8
PSA > 20 ng/mL

Treatment options - localized prostate cancer



External beam radiotherapy

Hormonal treatment

Interstitial: low or high dose rate

(robotic) surgery

WHAT DO YOU WANT?

QUALITY OF LIFE

1. BRACHYTHERAPY

RATIONALE for BRACHYTHERAPY

- Brachytherapy is the most conformal treatment modality
- Brachytherapy increases LC by delivering a higher radiation dose
  - Metabolic activity studies by MRI and MRI-spectroscopic imaging shows higher complete prostate metabolic atrophy and lower nadir PSA at 48 mths after PB vs EBRT
  - This higher intraprostatic tumor control is indicative of a positive therapeutic effect of the higher biological dose given with PB vs EBRT
- This observation is supported by clinical results from 3 RCTs of dose escalation using EBRT + PB vs EBRT

Morris et al, J Clin Oncol 2015;33-3
Hoskin et al, Radioth Oncol 2012; 103:217-222
Sathya et al, J Clin Oncol 2005; 23:1192-1199

- BT is considered as the ultimate dose escalation modality

- RCTs in PCA comparing EBRT with EBRT+PB in HR and high-tier IR PCA indicate further improvement of PSA recurrence free survival (20-30% at 7-10 years) with no documented CSS or OS benefit.

- However, recent publications using large databases indicate an increase in CSS and OS in PCA patients treated with any form of BT

- BT results in
  - Superior disease outcomes (mainly bPFS)
  - Higher complete prostate metabolic atrophy
  - Lower nadir PSA

Morris et al, J Clin Oncol 2015;33-3
Hoskin et al, Radioth Oncol 2012; 103:217-222
Sathya et al, J Clin Oncol 2005; 23:1192-1199
Shen et al, Int J Radiat Oncol Biol Phys 2012; 83:1154-1159
Amini et al, J Urol 2015;195:1453-1458
Picket et al, Int J Radiat Oncol Biol Phys 2006;65:65-72

Results

Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group

Peter Grimm[1], Ignace Billiet[2], David Bostwick[3], Adam P. Dicker[4], Steven Frank[5], Jos Immerzeel[6], Mira Keyes[7], Patrick Kupelian[8], W. Robert Lee[9], Stefan Machtens[10], Jyoti Mayadev[11], Brian J. Moran[12], Gregory Merrick[13], Jeremy Millar[14], Mack Roach[15], Richard Stock[16], Katsuto Shinohara[15], Mark Scholz[17], Ed Weber[18], Anthony Zietman[19], Michael Zelefsky[20], Jason Wong[21], Stacy Wentworth[22], Robyn Vera[23] and Stephen Langley[24]

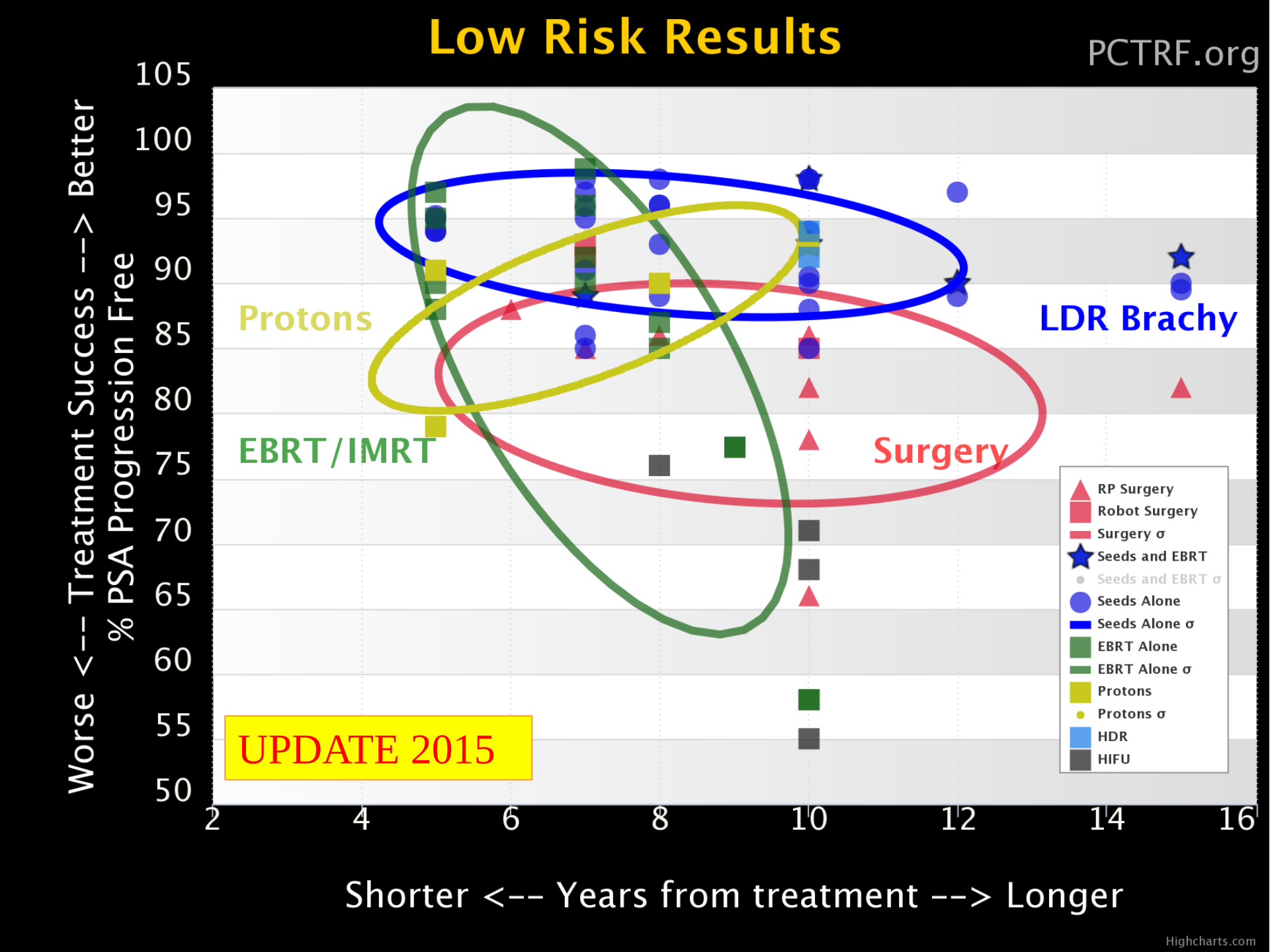
BJUI SUPPLEMENTS

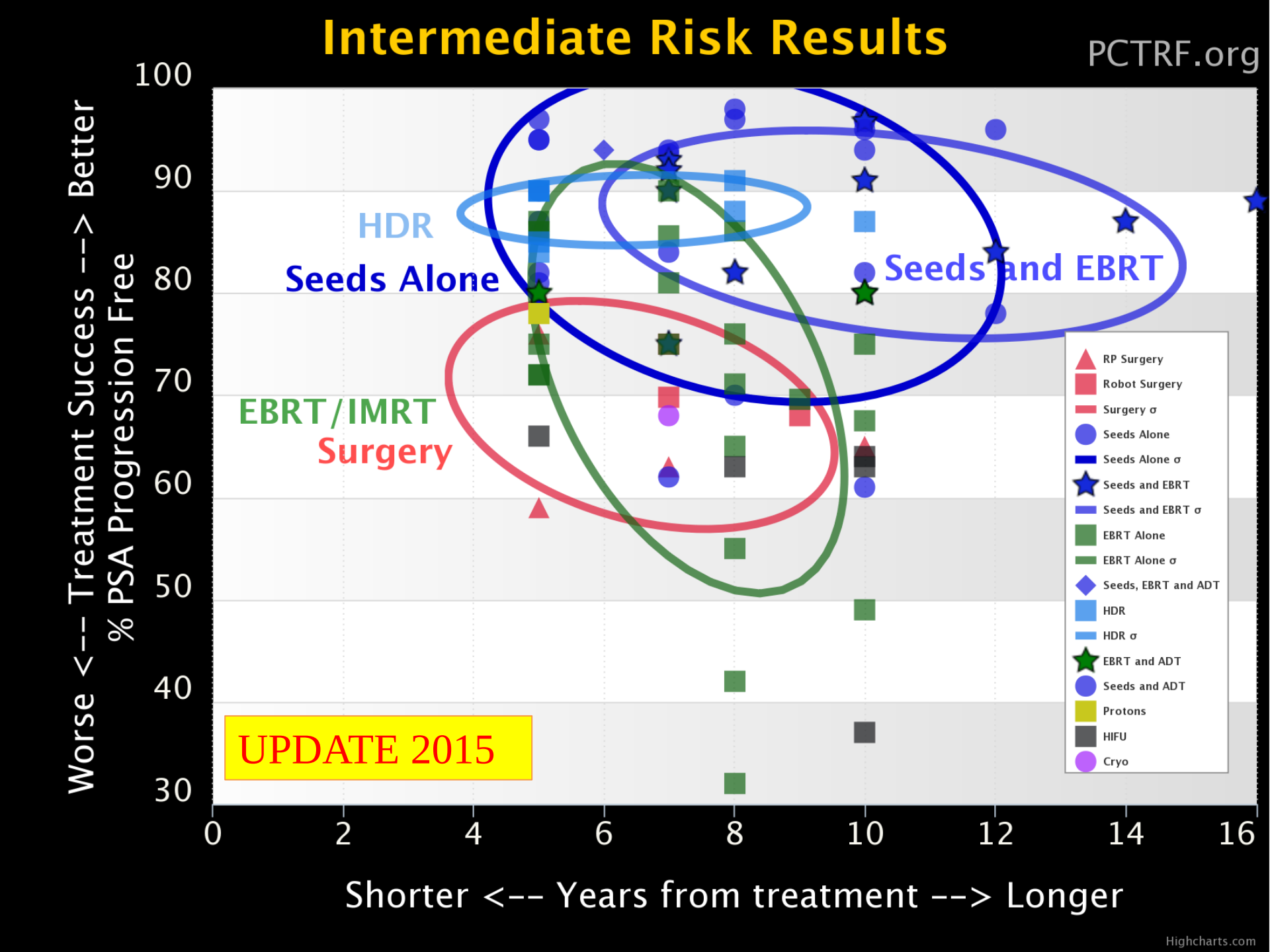
BJU INTERNATIONAL © 2012 BJU INTERNATIONAL | 109, SUPPLEMENT 1, 22–29

Literature review of all prostate cancer related papers published between 2000 and 2010

-5 strict criteria: - minimum/median follow-up of 5 years
- stratification into low, intermediate and high risk groups
- clinical (and pathological) stage
- accepted definition for prostatic specific antigen failure
- more than 100 patients in each risk group (high risk > 50)

18000 papers - 848 treatment related – 140 papers encountering these criteria


Low Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
105
100
95
90
85
80
75
70
65
60
55
50
2
4
6
8
10
12
14
16
Shorter <-- Years from treatment --> Longer
Protons
LDR Brachy
EBRT/IMRT
Surgery
UPDATE 2015
RP Surgery
Robot Surgery
Surgery σ
Seeds and EBRT
Seeds and EBRT σ
Seeds Alone
Seeds Alone σ
EBRT Alone
EBRT Alone σ
Protons
Protons σ
HDR
HIFU
Highcharts.com


Intermediate Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
% PSA Progression Free
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HDR
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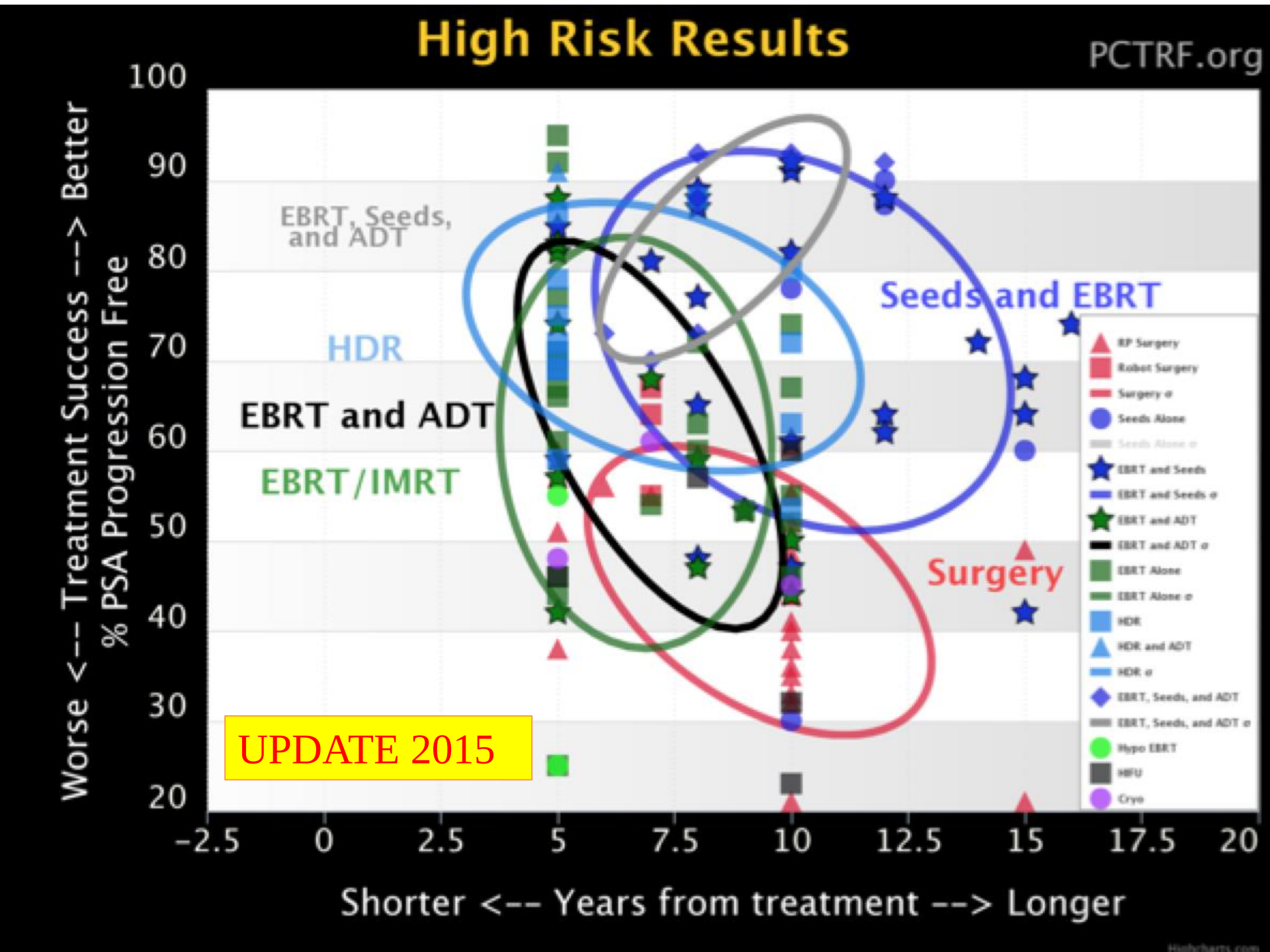
EBRT/IMRT
Surgery
UPDATE 2015
RP Surgery
Robot Surgery
Surgery σ
Seeds Alone
Seeds Alone σ
Seeds and EBRT
Seeds and EBRT σ
EBRT Alone
EBRT Alone σ
Seeds, EBRT and ADT
HDR
HDR σ
EBRT and ADT
Seeds and ADT
Protons
HIFU
Cryo
Highcharts.com


High Risk Results
PCTRF.org
Worse <-- Treatment Success --> Better
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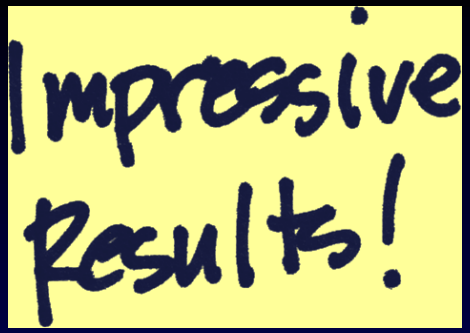
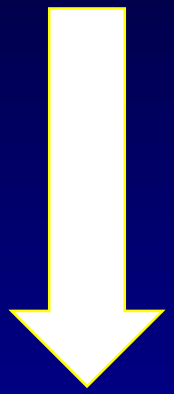
EBRT, Seeds, and ADT
HDR
EBRT and ADT
EBRT/IMRT
Seeds and EBRT
Surgery
UPDATE 2015
-2.5
0
2.5
5
7.5
10
12.5
15
17.5
20
Shorter <-- Years from treatment --> Longer
RP Surgery
Robot Surgery
Surgery σ
Seeds Alone
EBRT and Seeds
EBRT and Seeds σ
EBRT and ADT
EBRT and ADT σ
EBRT Alone
EBRT Alone σ
HDR
HDR and ADT
HDR σ
EBRT, Seeds, and ADT
EBRT, Seeds, and ADT σ
Hypo EBRT
HIFU
Cryo



Overall, patients treated with PB have exceptionally good long-term disease outcomes and compare favorably with other treatment modalities.

Results given in terms of biochemical control ….

However, this biochemical control depends on “local” control but also on “distant” control



What about the “local cure rates” after PB?

Patterns of Recurrence After Low-Dose-Rate Prostate Brachytherapy: A Population-Based Study of 2223 Consecutive Low- and Intermediate-Risk Patients

Andrea C. Lo, MD, W. James Morris, MD, FRCPC, Tom Pickles, MD, FRCPC, Mira Keyes, MD, FRCPC, Michael McKenzie, MD, FRCPC, and Scott Tyldesley, MD, FRCPC

"we estimate that the local recurrence rate of LDR-PB in our study cohort likely lies in the range of 1.8% to 2.7%."

10-YEAR EXPERIENCE WITH I-125 PROSTATE BRACHYTHERAPY AT THE PRINCESS MARGARET HOSPITAL: RESULTS FOR 1,100 PATIENTS

JUANITA CROOK, M.D.,* JETTE BORG, PH.D.,† ANDREW EVANS, M.D.,‡ ANTS TOI, M.D.,¶ E. P. SAIBISHKUMAR, M.D.,* SHARON FUNG, M.SC.,§ AND CLEMENT MA, M.SC.§

Thus, *the local relapse rate should range from 1.0% to 2.2%*, but it is likely to be closer to the biopsy-proven 1.0% of patients, because all other men with biochemical failure in this cohort had negative biopsy results

Distant and local recurrence in patients with biochemical failure after prostate brachytherapy

Richard G. Stock, Jamie A. Cesaretti, Pamela Unger, Nelson N. Stone

"Hence, at a median follow-up of 6.8 years, the local recurrence rate of the Mt. Sinai cohort treated with LDR-PB should fall between 1.3% and 4.5%"

Brachytherapy, 7 (2008), pp. 217–222

Patterns of failure after iodine-125 seed implantation for prostate cancer ☆

David S. Lamb [a,b,*], Lynne Greig [c], Grant L. Russell [d], John N. Nacey [a,d], Kim Broome [e], Rod Studd [d], Brett Delahunt [a], Douglas Iupati [b], Mohua Jain [f], Colin Rooney [c], Judy Murray [a], Peter J. Lamb [a], Peter B. Bethwaite [a]

"by combining the 0.2% who had local failure with the 2.2% whose site of failure was unknown, the local relapse rate should range from 0.2% to 2.4%"

Radiotherapy and Oncology 112 (2014) 68–71

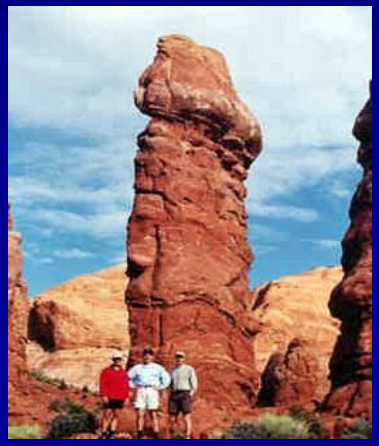
Cure

Prostate brachytherapy

Is highly effective

Local control is extremely high

Quality of Life – Side Effects



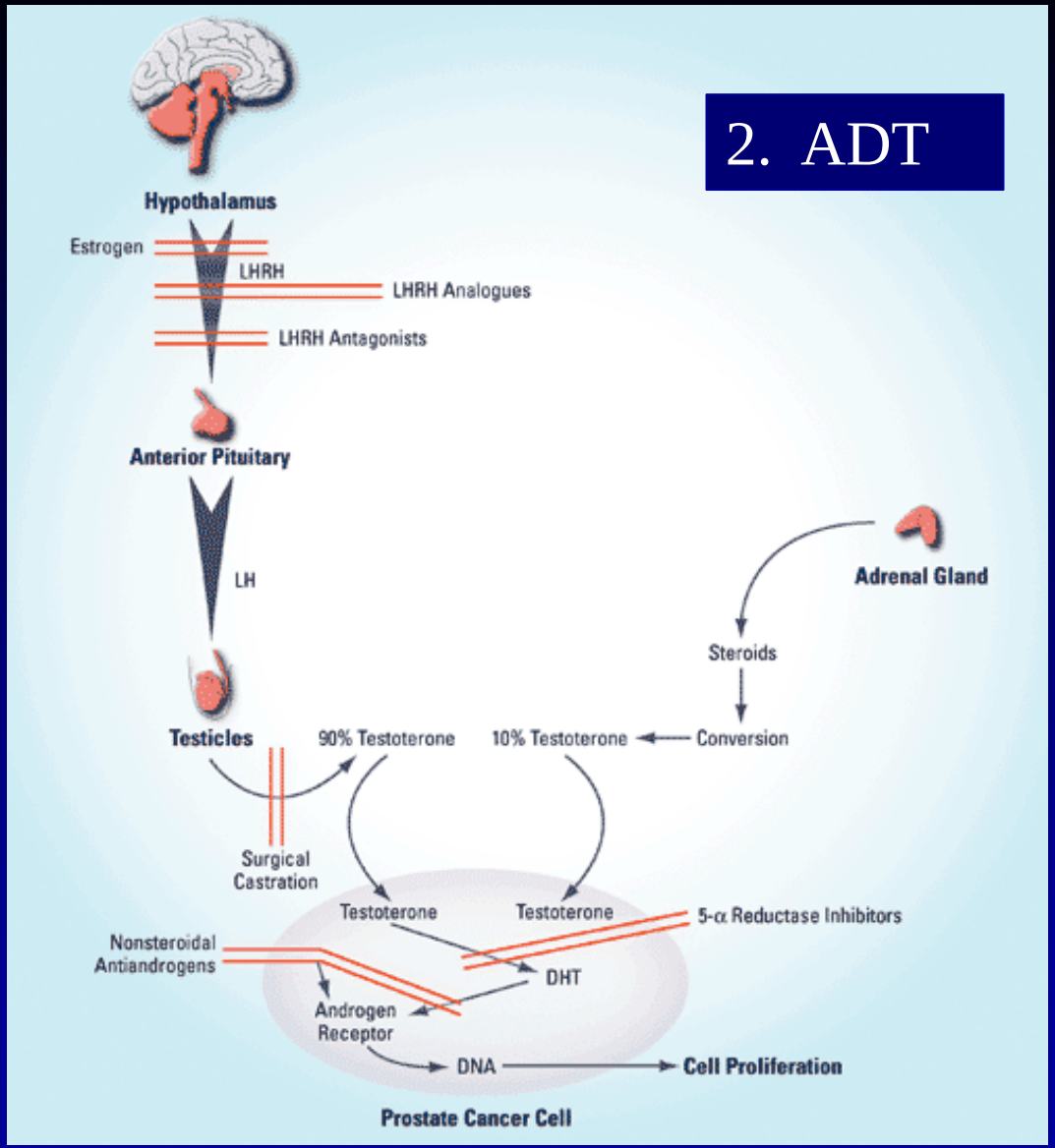
Quality of Life – Side Effects

Prostate brachytherapy

Toxicity is low and acceptable

No decrease in long term QoL

2. ADT

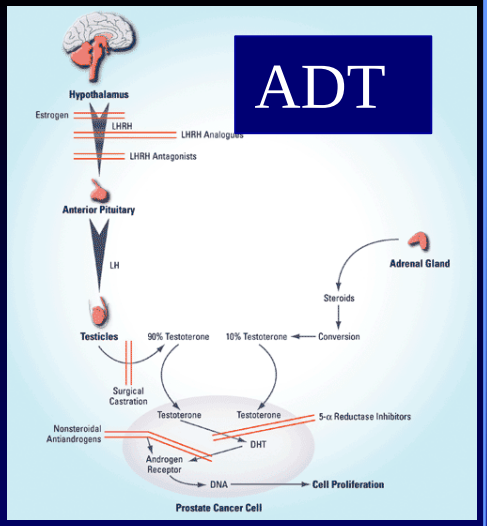

Hypothalamus
Estrogen
LHRH
LHRH Analogues
LHRH Antagonists
Anterior Pituitary
LH
Testicles
Adrenal Gland
Steroids
90% Testoterone
10% Testoterone
Conversion
Surgical Castration
Testoterone
Testoterone
5-α Reductase Inhibitors
Nonsteroidal Antiandrogens
DHT
Androgen Receptor
DNA
Cell Proliferation
Prostate Cancer Cell

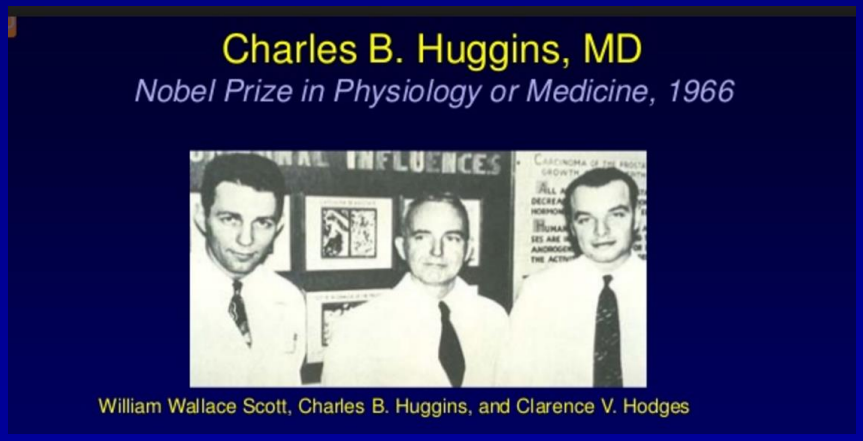
1940: Canadian born Charles Huggins recognized the androgen dependence of PCA

1966: nobel price for medecine: discoveries concerning hormonal treatment of PCA

1997: Zietman: the combination of radiation with orchiectomy for Shionogi tumors treated in vitro resulted in significant increase in control

Now, several large national and international RCT's confirmed and quantified the therapeutic benefit of ADT in combination with EBRT





Wolff FR et al: Eur J Cancer, 2015;51:2345-2367

The Seven Dwarves of ~~Menopause~~ **ADT**

Itchy, Bitchy, Sweaty, Sleepy, Bloated, Forgetful & Psycho

….. and they still have many other friends …

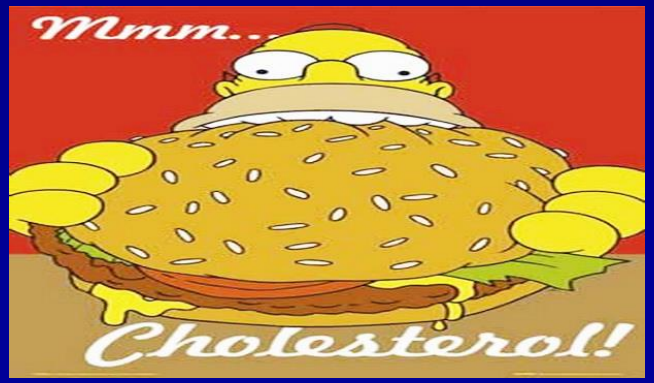
Well-documented side effets of ADT are:

- Sexual dysfunction
- Loss of libido
- Hot flashes
- Fatigue
- Decreased muscle mass
- Cognitive dysfunction
- Depression – where as up to 27% of patients on ADT may suffer psychiatric illness during their treatment

Well-documented side effets are:

- Increased risk of osteoporosis (23% increase in incidence of fractures)
- Increased incidence of metabolic syndrome (50% in ADT patients vs 20% in normal population - even with 1 year ADT)
- Central and peripheral obesity (9 – 11% increase in fat mass after 1 yr of ADT)
- Increase of total cholesterol (by 9%), Triglycerides (by 27%) and decreased HDL-cholesterol (by 11%) after only 3 mths of ADT
- Elevated blood pressure
- Elevate fasting glucose and fasting insulin
- Decrease insulin sensitivity and increase of diabetes

➔ All increasing the risk of a cardiovascular event and/or sudden cardiac death 12-60 mths after starting ADT



Even short time ADT can:

- negatively impact QOL
- increase morbidity
- increase mortality

Evidence shown in observational studies

This is however NOT confirmed in RCTs

(? inclusion of older, more frail patients – reports on non-fatal events?)

Voog et al Eur Urolo 2016;69:204-210
Sanda et al N Eng J Med 2008; 358:1250-1261
Beyer D et al Int J Radiat Oncol Biol Phys 2005; 61:1299-1305

PRIMARY CAUSES OF DEATH AFTER PERMANENT PROSTATE BRACHYTHERAPY

NATHAN BITTNER, M.D., M.S.,[†] GREGORY S. MERRICK, M.D.,[*] ROBERT W. GALBREATH, PH.D.,[*]
WAYNE M. BUTLER, PH.D.,[*] KENT E. WALLNER, M.D.,[†‡] ZACHARIAH A. ALLEN, M.S.,[*]
SARAH G. BRAMMER, B.S.,[*] AND MARK MOYAD, M.D., M.P.H.[§]

1354 patients – 5,4 years median FU – 51% ADT use

Primary causes of death in patients treated with PB (+EBRT) (+ADT)

- cardiovascular disease 42 %
- 30% other cancer 30 %
- Prostate cancer: 8,7 %

Patients with HR-disease had double the risk of dying from CVD compared with IR and LR

- HR: 19,8% vs IR 9,3% vs LR 8,7%

Excess morbidity and mortality is seen predominantly in patients with pre-existing cardiovascular co-morbidity

Bittner et al, Int J Radiat Oncol Biol Phys 2008;72:433-440

Nanda et al, JAMA 2009;302:866-873
Nguyen et al, Int J Radiat Oncol Biol Phys 2012;82:1411-1416

Even short term ADT gives an absolute increase 5,3% at 10 years ! (Kobutek et al)

Re-analysis of 6 RCTs (Albertsen et al)

- the increase in cardio-vascular mortality and morbidity might be an LHRH agonist class effect
- significantly less CVD events in men treated with LHRH antagonists vs LHRH agonists (HR: 0,44 - 95% CI 0,26-0,74 - p=0,002)

Pronounce NCT02663908: RCT comparing major CV events with LHRH agonists vs antagonists in patients with pre-existing CV morbidity

Kobutek et al, Int J Radiat Oncol Biol Phys 2014;90:S15
Albertsen et al, Eur Urol 2014;65:565-573

3. EBRT + ADT

RATIONALE for combining EBRT and ADT:

-(neo-adjuvant ADT) improves the geometry of the prostate target by decreasing the volume juxtaposed to adjacent OAR

-If given before EBRT (in experimental setting), the anti-angiogenesis effect of ADT may

- 'normalize' the vasculature and lead to better perfusion
- increase the oxygenation
- increase the radiation tumor sensistivity
- increase the LC. Reducing local failure may reduce second-wave metastatic spread and thus improve OS

-The synergistic relationship in concurrent administration might produce a biologic advantage

-Several RCTs show an improvement in bPFS and LC but also in DSS and 0S … so … ADT might have an influence on local and systemic disease

-Clinical evidence supports the hypothesis that ADT can eliminate subclinical micro-metastases.

- Addition of ADT to EBRT, RCTs have shown benefit in improving OS, CSS and bPFS in HR
  - RTOG 85-31 - RTOG 92-02 - TROG 96-01
  - RTOG 86-10 - RTOG 94-08 - EORTC 22961
  - EORTC 22863 - Harvard/DFCI - TROG 96-01
- Addition of ADT to EBRT, RCTs have shown benefit in improving OS, CSS and bPFS in IR
  - RTOG 94-08
  - Harvard/DFCI 95-096

- A Spanish RCT showed even in a dose escalation to 78 Gy, 24 vs 4 months of ADT improves bPFS, metastatic-free survival and OS in patients with IR and HR disease.

- It is clear that ADT has an additive effect on improving disease outcomes with EBRT even at high doses of 78 or 81 Gy

  Optimal duration with EBRT for each risk category has not been established

Zapatero et al, Lancet Oncol; 2015;16:320-327
Zelefsky et al, Eur Urol: 2011; 60; 60:1133-1139

REFLECTIONS:

- The benefit of ADT in combination with EBRT (even with dose-escalated EBRT) may be because of compensation for suboptimal radiation dose and less effective therapy.

- Because of the very high intraprostatic dose and excellent disease control, ADT is likely to have less biologic effect with PB, except perhaps in cases with very high-volume diesease or through spatial cooperation for suppression of micrometastic disease

- Addition of ADT to PB in IR and HR patients has been shown to decrease 2-yr post PB positive biopsy rate from 14% to 3,5%

Lo et al, Int J Radiat Biol Phys, 2015;91:745-751
Stone et al, Int J Radiat Biol Phys, 2010; 76:355-360
Stone et al: Mol Urol 2000; 4(3): 163-168

REFLECTIONS:

If we disregard normal tissue tolerance, one can speculate that any truly localized PCA can be cured with radiation alone, given suffisiently high dose and ensuring complete coverage of the tumortarget.

4. Do we need ADT in addition to PB ?

Cytoreduction

- The aim is to downsize the prostate
- Most common used is a LHRH agonist
- Alternative: dutasteride and bicalutamide
  - RCT shows a non-inferiority of this regimen in comparaison with LHRH
  - So because of the potential impairment of QoL associated with ADT, one may consider the less toxic combination fo 5-&-reductase inhibitor + oral anti-testosterone for cytoreduction.
- No improved oncologic outcome

Gaudet et al; Brachytherapy 2015;14:S33-34
Ciezki et al; Int J Radiat Oncol Biol Phys 2004;60:1347-1350
Potters et al; J Urol 2005;173:1562-66
Ohashi et al; Radioth Oncol 2013;109:241-245
Morris et al; Cancer 2013; 119:1537-1546
Martin et al; Int J Radiat Oncol Biol Phys 2007:67:334-341

American Brachytherapy Society Task Group Report: Use of androgen deprivation therapy with prostate brachytherapy—A systematic literature review

M. Keyes[1,*], G. Merrick[2], S.J. Frank[3], P. Grimm[4], M.J. Zelefsky[5]

In this review: studies grouped based on risk stratification

Low Risk and favourable Intermediate Risk

5 studies

- 4 studies describing outcome in patients treated with LDR +/- ADT
- 1 study describing outcome in patients treated with LDR +/- EBRT +/- ADT

ADT used in 27-65% of patients
ADT duration 3-6 mths

Most often: downside prostate volume before BT and in one study for IR features

- None of the studies showed any benefit from ADT to bPFS.
- Effect on CSS not reported
- Not associated with improved or detrimental OS

Ciezki *et al.* (70)	Multi-institutional, USA	1996—2001	1668
Potters *et al.* (71)	New York Institutions, USA	1992—2000	1449
Ohashi *et al.* (72)	Multi-institutional Japan	2003—2009	663
Morris *et al.* (73)	British Columbia, Canada	1998—2003	1006
Martin *et al.* (74)	Quebec City Canada	1994—2001	396

Intermediate Risk

6 studies describing outcome in patients treated with LDR +/- ADT or LDR +/- EBRT +/- ADT (5854 patients)

ADT used in 17-81% of patients
ADT duration 4 months

Results:

- bPFS:
  - 4 studies: no overall benefit with ADT
  - 2 studies: no report on bPFS
- CSS:
  - 1 study shows an absolute 2% benefit on CSS with ADT
  - 1 study shows a benefit in unfavourable IR patients
  - 1 study shows a benefit if BED < 150 Gy
- OS:
  - 4 studies did not report on the association between ADT and OS
  - 1 study showed no benefit

Rosenberg *et al.* (75)	Chicago	1997–2007	807
Tran *et al.* (76)	Multi-institutional, UK	2003–2007	615
Ho *et al.* (77)	Mount Sinai, NY	1990–2004	558
Keane *et al.* (78)	Harvard, Boston, MA	1997–2013	2510
Bittner *et al.* (79)	Multi-institutional, USA	1995–2001	932
Stock *et al.* (80)	Mount Sinai, NY	1994–2006	432

Intermediate and High Risk

8 studies describing outcome in patients treated with mono(brachy-)therapy or combination therapy

- 6 LDR – 1 HDR and 1 HDR or LDR
- ADT used in 32-66% of patients
- ADT median duration 6 months (4-28 months)

LDR			
Lee (81)	Mount Sinai, NY	1990–1998	201
Strom (82)	Tampa, FL	2001–2011	120
Merrick *et al.* (83)	Multi-institutional, USA	1995–2003	530
Merrick *et al.* (84)	Multi-institutional, USA RCT—20 vs. 44 Gy EBRT + PB	1999–2004	247
Dattoli *et al.* (85)	Multi-institutional, USA	1992–1997	321
Merrick *et al.* (86)	Multi-institutional, USA RCT—0 vs. 20 vs. 44 Gy EBRT + PB	1999–2013	630
HDR/LDR			
Kraus *et al.* (87)	William Beaumont	1991–2004	1044 Patients
HDR			
Schiffmann *et al.* (88)	Hamburg Germany	1999–2009	392

Results:

•bPFS:

- 6 (out of the 8) studies: no benefit with ADT except in patients with low D90
- 1 (HDR) study showed 12% (in IR disease) and 20% (in HR disease) benefit to adding ADT

•CSS:

- None of the studies showed overall benefit

•OS:

- None of the studies showed overall benefit

High Risk

11 studies describing outcome in patients treated with combination therapy

- 10 LDR + EBRT and 1 HDR + EBRT
- 1 included also patients treated by LDR PB alone
- ADT used in 40-91% of patients
- ADT median duration 3-12 months

LDR			
Ohashi *et al.* (89)	Japan	2003–2009	206
Bittner *et al.* (56)	Multi-institutional, USA (very high risk)	1995–2007	131
Bittner *et al.* (90)	Multi-institutional, USA	1995–2005	186
Wattson *et al.* (91)	Multi-institutional, USA	1991–2007	2234
D'Amico *et al.* (92)	Multi-institutional, USA	1991–2005	1342
Merrick *et al.* (93)	Multi-institutional, USA	1995–2002	204
Shilkurt *et al.*(94)	Multi-institutional, USA	1995–2010	448
Merrick *et al.* (55)	Multi-institutional, USA	1995–2005	284
Liss (95)	Multi-institutional, USA	1998–2008	141
Fang *et al.* (96)	Multi-institutional, USA	1995–2005	174
HDR			
Prada *et al.* (97)	Oviedo, Spain	1998–2006	252

Results:

- bPFS: 9 studies showed an association between ADT and bPFS
  - 6 showed a benefit with ADT (2 studies showed a 13% benefit with longer ADT duration)
  - 3 showed no benefit with ADT
- CSS: 9 studies showed an association between ADT and CSS
  - 3 showed a benefit with ADT
  - 6 showed no benefit with ADT
- OS: 5 studies reported on an association between ADT and OS
  - None of the studies showed an overall benefit

LR – IR - HR

A lot of studies describe outcomes in all risk categories
In the ABS review: 22 studies – 23.180 patients
16 using LDR (20991 patients) – 5 using HDR (2189 patients)
Median FU: 3,8 – 10 years
ADT use: 18 – 83 % - median duration: 3 – 9 months

Results:

- bPFS: 16 studies showed an association between ADT and bPFS
    - 4 showed a benefit with ADT
        - 1 study reported a 15% benefit only with longer ADT duration
        - 1 study reported a 24% benefit only if BED was < 150 Gy
        - 1 study reported a 9-15% benefit only in HR disease
    - 12 showed no benefit with ADT (including all HDR studies)
    - Remark: one study showed a detriment to bPFS with the addition of ADT in IR disease

LR – IR - HR

Results:

- CSS: 7 studies showed an association between ADT and CSS
    - All 7 showed no benefit with ADT
- OS: 6 studies reported on an association between ADT and OS
    - 3 studies showed no impact on OS
    - 3 showed a statistically detriment to OS using ADT
    - One showed a trend to worse OS

- 6 ongoing RCTs evaluation the role of ADT with PB in IR and HR patients
- Only one completed RCT adressed (at least indirectly) the role of ADT in PB

Australian multicenter TROG 03.04 RADAR 2 x 2 factorial RCT in men with locally advanced PCA

–1071 men

–randomization to receive ADT for 6 to 18 months with dose-escalated EBRT (66-70-74 or 46 Gy + HDR 19,5 Gy in 3 fractions) and also randomized between 0 and 18 months of Zoledronic Acid

–Primary endpoint bPFS subsequently changed to a PCSM. Median follow-up: 7,4 years

–No significant difference in PCSM or OS

–However: 18 months of ADT had a positive effect on the PSA and LC outcome on all EBRT dose levels with greater benefit in lower doses and had almost NO effect for patients treated with HDR boost (absolute difference 3%)

–This data suggest minimal (if any) benefit to longer ADT using PB – however, it does not answer the question if ADT is needed with PB at all

Denham et al; Radiother Oncol 2015;15:1076-1089

Literature shows significant heterogeneity

- of the patient populations
- in the risk categories
- in the definition of risk factors
- in the follow-up time
- in ADT administration
- in the duration for ADT administration

The retrospective analyses induces unavoidable patient selection and treatment selection bias !

	bPFS	CSS	OS
Total studies 52	Reported in 42 studies (80%)	Reported in 24 studies (46%)	Reported in 19 studies (36%)
Benefit to ADT	12 (28%)	4 (16%)	0
No benefit	30 (71%)	19 (79%)	16 (84%)
Detriment with ADT	1 (2%)	—	3 (15%)

High–intermediate prostate cancer treated with low-dose-rate brachytherapy with or without androgen deprivation therapy

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PURPOSE: To describe outcomes of men with unfavorable (high-tier) intermediate risk prostate cancer (H-IR) treated with low-dose-rate (LDR) brachytherapy, with or without 6 months of androgen deprivation therapy (ADT).

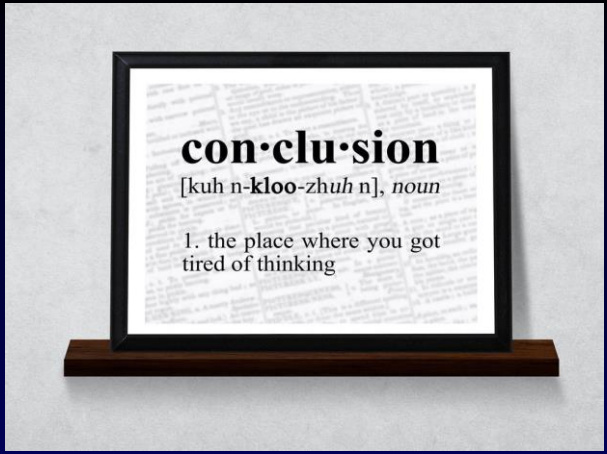
CONCLUSIONS: The addition of 6 months of ADT to LDR brachytherapy for H-IR prostate cancer does not improve 5 year prostate specific antigen control, and we no longer routinely recommended it.

"THE SECRET OF CHANGE IS TO FOCUS ALL OF YOUR ENERGY, NOT ON FIGHTING THE OLD, BUT ON BUILDING THE NEW."

– SOCRATES

- No clinical or biochemical benefits from the addition of ADT in LR en fIR

- Beneficial in bPFS
  - in most patients with HR disease using LDR
  - some patients with uIR
  - In patients with low D90 or low BED



- Not beneficial in CSS
  - A very small absolute benefit (2%) to CSS was found in only a few studies and was predominantly with 3-modality treatment vs PB monotherapie

- No OS survival benefit was found in any study

- However: three studies reported on a detriment to OS using ADT (cave: older patients, existing CV disease)

- With high-quality brachytherapy, the dose is sufficient so that any synergistic local effect of ADT with radiation is likely to be of little benefit (unless high volume disease *perhaps …*)
- uIR and HR: ADT is likely to play a role through spatial cooperation for suppression of micro-metastatic disease
- Duration in addition to BT: none or short(er) than with EBRT


THANK
YOU!